sustained virologic response (SVR) rates with the currently approved interferon-based therapies, these therapies are limited by the on-treatment side effects and by the relatively inferior response in patients with HCV genotype 1 infection. Several host and viral factors have been implicated to influence the disease progression and the treatment response in chronic hepatitis C (CHC) patients, and efforts to modify these factors to the optimize the therapeutic response are ungently needed.

Recently, host metabolic factors, such as diabetes mellitus (DM), insulin resistance (IR), hepatic steatosis, and impaired lipid metabolism have been found to closely associated with HCV infection. Ample clinical evidence indicate that deranged lipid profiles and hepatic steatosis correlate with HCV infection, suggesting their potential roles of predicting therapeutic responses. Furthermore, it has been demonstrated in vitro that the lipid rafts, mainly composed of cholesterol and sphingolipid, and the lipid droplet, an organelle for storing neutral lipids, play the crutial roles of producing infectious viruses. While HCV genotypes 3 virus may directly cause hepati steatosis, the association of viral loads in HCV genotype 1 or 2 virues, the mainly types in infected individuals in the world, with the lipid profiles still remains elusive. The search of the association between lipid profiles and the HCV genotypic differences is therefore important.

A recent study recruting 531 patients with either HCV genotype 1 or 2 infection showed that high serum triglyceride, totoal cholesterol and low-density lipoprotein (LDL) correlated with high HCV RNA levels. In patients with low body mass index (BMI), high modeal assessment of insulin resistance index (HOMA-IR) and total cholesterol levels were associated with high HCV viral load. After stratification by HCV genotypes, lipid profiles were highly associated with HCV viral load in genotype 2, rather than genotype 1 patients. The study indicated that differed mechanisms of deranged lipid profiles between HCV genotype 1 and 2 viruses. Because the casual relationship of the viral load and the lipid profiles are still to be determined, manipulation of the lipid profiles aiming in improving the anti-HCV therapy deserves further studies.

Concurrent Session 5 – Gram-Negative Bacterial Infections and Resistance

CS5-01 Complete Genome Sequence and Proteome of *Laribacter hongkongensis*, a Novel Bacterium Associated with Gastroenteritis and Traveler's Diarrhea

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Despite extensive investigations, a microbiological cause cannot be found in about half of the patients with infectious disease. Throughout the years, scientists have spent tremendous efforts in looking for microorganisms associated with these "unexplained infectious disease syndromes". In 2001, we discovered *Laribacter hongkongensis* gen. nov. sp. nov., a facultative anaerobic, Gram-negative, S-shaped, urease-positive rod of the *Neisseriaceae* family, from blood and empyema thoracis of a patient with alcoholic cirrhosis. During the past eight years, we have documented that *L. hongkongensis* was associated with community acquired gastroenteritis and traveler's diarrhea and cases were found globally in patients who resided in or had recent travel histories to countries in Asia, Europe, America and Africa. We have found that freshwater fish is the reservoir and it was also found in Chinese tiger frogs and drinking water reservoirs. Due to the potential of its clinical importance and related ecology, important phenotypic characteristics and phylogenetic position, and the availability of genetic manipulation systems for downstream experiments, we sequenced the complete genome of *L. hongkongensis*, with the aim of achieving better understanding of its biology, mechanism of adaptation to different hosts, and virulence mechanisms. The complete genome sequence of *L. hongkongensis* consists of a 3,169-kb chromosome with G+C content of 62.35%. Genome analysis reveals different mechanisms potentially important for its adaptation to diverse habitats of human and freshwater fish intestines and freshwater environments. The gene contents suggest that amino acids and fatty acids can be used as carbon sources. The extensive variety of transporters including multidrug efflux and heavy metal transporters, as well as genes involved in chemotaxis may enable *L. hongkongensis* to survive in different environmental niches. Genes encoding urease, bile salts efflux pump, adhesin, catalase, superoxide dismutase and other putative virulence factors, such as hemolysins, RTX toxins, patatin-like proteins, phospholipase A1 and collagenases, are present. Proteomes of *L. hongkongensis* cultured at 37°C and 20°C showed differential gene expression, including two homologous copies of *argB*, *argB*-20 and *argB*-37, that encode two isoenzymes of *N*-acetyl-L-glutamate kinase (NAGK), NAGK-20 and NAGK-37, in the arginine biosynthesis pathway. NAGK-20 showed higher expression at 20°C whereas NAGK-37 showed higher expression at 37°C. NAGK-20 also had a lower optimal temperature for enzymatic activities and was inhibited by arginine probably as negative feedback control. Similar duplicated copies of *argB* are also observed in bacteria from hot springs, including *Thermus thermophilus*, *Deinococcus geothermalis*, *Deinococcus radiodurans* and *Roseiflexus castenholzii*, suggesting that similar mechanisms for temperature adaptation may be employed by other bacteria.

CS5-02 Resistance Trends and Treatment Options of Infections of Gram-negatives

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Increasing antimicrobial resistance brings difficulties for selection of effective antimicrobial regimens in the treatment of bacterial infections. Antimicrobial resistance trends and therapeutic options will be discussed for the following highly antimicrobial resistant gram-negative bacilli: ESBL-producing *Escherichia coli* and *Klebsiella pneumoniae*, and multiple-resistant *Pseudomonas aeruginosa* and *Acinetobacter baumannii*. ESBLs-producing strains of *E. coli* and *K. pneumoniae* have been increasing and currently approximately half of the strains produce ESBLs in China. Carbapenems produce the best outcomes in the treatment of ESBLs infections. *In vitro* ESBL-producing organisms vary in their susceptibility to other antimicrobials. The susceptibility rates of ESBL-producing strains are relatively high to β-lactamase inhibitor combinations such as cefoperazone-sulbactam and piperacillin-tazobactam, which might be used in the treatment of such infections in high dosage. The isolation of *P. aeruginosa* and *A. baumannii*, the most common pathogens in ventilator-associated pneumoniae (VAP), has been increasing in clinical specimens. Both *P. aeruginosa* and *A. baumannii* are non-fermenters, which are highly resistant to antimicrobial agents. According to a bacterial surveillance program, CHINET, in China, the resistance rates of *P. aeruginosa* clinical strains to ceftazidime, piperacillin-tazobactam, imipenem, meropenem and ciprofloxacin were from 21% to 30% in 2008, while the resistance rates were relatively lower to amikacin, cefepime and cefoperazone-sulbactam with resistance rates from 15% to 18%. *Acinetobacter* spp. was more resistant to most antimicrobials than did *P. aeruginosa*. The choice of antimicrobial agents should be based on the *in-vitro* susceptibility results. For severe infections, combination therapy is recommended as following: an active β-lactam combined with an aminoglycoside or with a quinolone such as ciprofloxacin or levofloxacin. *A. baumannii* is highly susceptible to doxycycline or minocycline, but the clinical experience is limited. Colistin has emerged again as a therapeutic option for pandrug resistant (PDR) *P. aeruginosa* and *A.*